Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis

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Background: Allergic Rhinitis and its Impact on Asthma in collaboration with the World Health Organization initiative reclassified allergic rhinitis, like asthma, by duration and severity. The Xyzal in Persistent Rhinitis Trial is the first large, long-term clinical trial studying patients with persistent rhinitis as defined by Allergic Rhinitis and its Impact on Asthma.
Objectives: Two primary objectives were defined: comparison of the Rhinoconjunctivitis Quality of Life Questionnaire overall score and Total 5 Symptoms Score (rhinorrhea, sneezing, nasal congestion, and nasal and ocular pruritus) over a period of 4 weeks between levocetirizine 5 mg and placebo. Secondary endpoints included similar evaluations at 1 week and 3, 4.5, and 6 months, summary scores for a general health status questionnaire (Medical Outcomes Survey Short Form 36), a pharmacoeconomic assessment, comorbidities, and a safety evaluation.
Methods: The Xyzal in Persistent Rhinitis Trial was a 6-month double-blind, placebo-controlled, multicenter, multinational trial in 551 patients. Adults with persistent rhinitis sensitized to both grass pollen and house dust mite were randomized to receive levocetirizine 5 mg/d or placebo.
Results: A total of 421 patients completed the full study. Levocetirizine significantly improved both the Rhinoconjunctivitis Quality of Life Questionnaire overall score and the Total 5 Symptoms Score from week 1 to 6 months (all *P* values <.001). Medical Outcomes Survey Short Form 36 summary scores were also improved in the levocetirizine group compared with the placebo group. Treatment cessation because of lack of effect, comorbidities, and overall costs of disease, and comorbidities per working patient per month (€160.27 vs €108.18) were lower in the levocetirizine group.
Conclusion: Levocetirizine was shown to improve quality of life and symptoms and to decrease the overall costs of the disease over the 6-month treatment period. (J Allergy Clin Immunol 2004;114:838-44.)

Key words: ARIA, persistent allergic rhinitis, health-related quality of life, levocetirizine, long-term therapy, pharmacoeconomics

Allergic rhinitis is a global health problem of increasing prevalence, affecting between 10% and 40% of the world's population.[1,2] In some countries it is now approaching epidemic proportions and is becoming a significant public health concern.[3] The cumulative symptoms of allergic rhinitis can be troubling[4] and may impair daily activities and sleep patterns, resulting in a significant effect on patients' health-related quality of life (HRQoL),[5-7] learning, and psychomotor performance,[8] and thereby in an economic effect on society in terms of both direct and indirect costs.[9] Rhinitis is also associated with other conditions such as asthma, sinusitis, and otitis media.[10-14] The Allergic Rhinitis and its Impact on Asthma (ARIA) project has developed the rhinitis disease classification and management guidelines to supersede the previous imprecise *seasonal* and *perennial* categories. Persistent allergic rhinitis is defined by the presence of symptoms for more

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Abbreviations used
ARIA: Allergic Rhinitis and its Impact on Asthma
HRQoL: Health-related quality of life
ITT: Intention to treat
RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire
PER: Persistent rhinitis
SF-36: Medical Outcomes Survey Short Form 36
T5SS: Total 5 Symptom Score
XPERT: Xyzal in Persistent Rhinitis Trial

than 4 days per week and for more than 4 weeks per year. Corollary, intermittent allergic rhinitis is defined by the presence of symptoms lasting less than 4 days per week or less than 4 weeks per year.

Levocetirizine (XYZAL; UCB Pharma, Brussels, Belgium) is a new oral, nonsedating H_1-antihistamine that has been shown to be effective against allergic symptoms while offering good tolerability,[15-20] and was therefore selected as the active treatment in this persistent rhinitis (PER) trial designed by an expert board, which consists largely of ARIA members. The Xyzal in Persistent Rhinitis Trial (XPERT) used a comprehensive battery of clinical, HRQoL, and pharmacoeconomic assessments, applied over the long term and using electronic diary cards, where appropriate, to enhance data capture.

There were 2 primary objectives for this study. The first was to compare the effects of levocetirizine and placebo on HRQoL, as measured by the change from baseline of the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) overall score after 4 weeks of treatment. The second primary objective was to compare the mean Total 5 Symptoms Score (T5SS; sum of rhinorrhea, sneezing, nasal congestion, and nasal and ocular pruritus; score, 0-15), evaluated for 24 hours over a period of 4 weeks of treatment.

Secondary objectives were to compare RQLQ overall score and symptom scores over periods of 1 week and 3, 4.5, and 6 months of treatment. Additional secondary objectives were to compare the effects on health status as measured by means of the Medical Outcomes Survey Short Form 36 (SF-36) questionnaire (physical and mental summary scores) over periods of 4 weeks, 3 months, 4.5 months, and 6 months, and to compare the rescue medication use over the 6-month treatment period and to assess the overall safety of levocetirizine over the 6-month study period.

The study also provided pharmacoeconomic data on the treatment of PER. It is the first long-term (6-month) trial performed with an H_1-antihistamine in PER and following a large multicenter design involving more than 500 patients throughout 5 European countries.

METHODS

This study was conducted according to an exacting protocol, based largely on ARIA guidelines for rhinitis. The study was performed in 5 European countries (Belgium, France, Germany, Italy, and Spain) as a multicenter, randomized, placebo-controlled, double-blind, parallel group trial, designed to investigate several related aspects of PER.

TABLE I. Study objectives*

	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
	1 wk	4 wk	3 mo	4.5 mo	6 mo
RQLQ overall score	2	1	2	2	2
Mean T5SS	2	1	2	2	2
Individual rhinitis symptoms	E	E	E	E	E
SF-36 physical and mental summary scores		2	2	2	2
Rescue medication use (E)	Measured over the whole duration of the study				
Safety of levocetirizine (2)	Measured over the whole duration of the study				
Pharmacoeconomics (E)	Measured over the whole duration of the study				

1, Primary objective; *2*, secondary objective; *E*, exploratory objective.
*Visit 1, selection; visit 2, randomization (baseline); visit 8, follow-up visit.

Schedule and inclusion criteria

At an initial assessment visit, male or female patients were considered for inclusion if they were older than 18 years, with symptoms of rhinitis present during the pollen season and on house dust exposure (PER defined as rhinitis lasting 4 days or more per week for 4 consecutive weeks or more per year). They also had to show a positive skin test (wheal >3 mm larger than the diluent control) or, if a skin test was not possible for a medical reason, specific serum IgE (CAP System, Pharmacia Diagnostic, Uppsala, Sweden) for at least house dust mite and 1 pollen allergen (grass or *Parietaria*, IgE level >3.5 U/mL).

Treatments were allocated to subjects by means of a randomization list prepared by UCB Pharma (blocks of 4).

Patients were enrolled at a randomization visit 1 week later if their symptoms were sufficient—that is, showing a combined symptom T5SS >6 of 15 for at least 4 days during the run-in period. Subjects were randomized to receive either levocetirizine 5 mg or placebo orally each evening, starting on the evening of the second visit and continuing for 6 months thereafter. Additional criteria for enrollment into this 6-month study were the ability to understand and complete electronic diaries and questionnaires. All randomized patients were assessed at the end of the first treatment week and again at weeks 4, 12, 18, and 26 before leaving the study at week 27 after an additional week's follow-up (Table I).

Exclusion criteria

Pregnant patients, nursing mothers, and women of childbearing age not using a medically accepted method of contraception were excluded, as were patients with an ear, nose, or throat or eye infection during the 2 weeks preceding the initial visit, and patients with asthma requiring daily treatment with other than an inhaled β-agonist as needed. Patients were also excluded if, among other diseases, they had atopic dermatitis or urticaria requiring antihistamine or corticosteroid treatment; an associated ear, nose, or throat disease such as vasomotor rhinitis or nasal polyps; other clinically significant diseases such as glaucoma or cardiovascular or hepatic diseases; or any condition likely to disturb absorption, distribution, metabolism, or excretion of the investigational drug.

Rescue medication

In cases of insufficient therapeutic response after at least 1 week of randomization and treatment, patients were permitted nasal or ocular cromoglycate in amounts limited to the least needed. In addition, in case of unbearable worsening of the symptoms linked to allergic rhinitis, after a minimum of 4 weeks of treatment (ie, after visit 4), patients were permitted a maximum of 20 mg oral prednisolone once daily for 5 days, for a maximum of 2 prednisolone courses during the study. All rescue medication use was carefully recorded, and compliance for both study and rescue medications was calculated at each visit, before dispensing new drug.

Ethical aspects

Informed consent was obtained from all participants, and the study was conducted in accordance with good clinical practice (Committee for Proprietary Medicinal Products/International Conference on Harmonization/135/95) and the revised Helsinki Declaration of 1996, and with the permission of the respective institutional review boards.

Assessment parameters

Health-related quality of life is a significant parameter because it considers the effect of both illness and treatment on a patient's life as perceived by the patient. Besides generic HRQoL questionnaires, disease-specific instruments can be used, which are often more sensitive.[21,22]

The RQLQ is a disease-specific, validated, and reproducible instrument for evaluating HRQoL on the basis of how symptoms and treatments affect each patient's physical, social, and emotional well-being.[23] It includes 28 items related to 7 domains. All of the items are averaged in an overall score ranging from 0 (no trouble) to 6 (major impairment). The RQLQ was completed by each subject at the start of visit 2 (randomization), and then at visits 3 to 7, or at the end of the study treatment in case of withdrawal (Table I).

The second instrument (SF-36) is a well-validated questionnaire to measure health status. The SF-36 is a generic measure—that is, it does not target a specific age, disease, or treatment group. As such, the SF-36 has been widely used to assess the relative burden of various diseases, including allergic rhinitis,[24] and to compare the effects of different treatments. Across 36 questions, it measures 8 health dimensions domains condensed into 2 physical and mental health summary measures, with scores ranging from 0 (worst reported health status) to 100 (best reported health status).[25] At each visit, except visit 3 (week 1), the SF-36 was completed by patients immediately after the RQLQ.

Rhinitis symptoms were assessed by using the T5SS. This total symptom score measures not only the typical symptoms normally responding to antihistamines, such as rhinorrhea, sneezing, and nasal and ocular pruritus, but also nasal congestion, which is, in practice, 1 of the most bothersome symptoms for patients with allergic rhinitis. Rhinitis symptoms were evaluated each day of the study by means of the electronic diary by using a 4-point scale from 0 (absent) to 3 (severe) for each symptom (Minidoc; Arnaced, Sittingbourne, United Kingdom). The use of electronic diaries promotes and monitors the daily recording of symptoms, thanks to alarm clock reminders for completion and prompts for missing data, thus avoiding the parking lot retrospective guesswork that is often involved in completion of a backlog of paper forms just before a clinic visit.

Pharmacoeconomic investigations included estimates for direct medical cost and indirect cost parameters in the working population (69%) related to PER and to comorbidities including asthma, sinusitis, otitis media, and upper respiratory infections. The direct costs consisted of the use of medical resources such as hospitalization, physician visits, and concomitant medications for investigated conditions. By using the World Health Organization adverse reaction terminology, the verbatims of the study were allocated to specific conditions, before unblinding, to categorize PER and comorbidities resources and events. Estimates for indirect cost parameters related to PER or comorbidities—measured through a weekly questionnaire on Minidoc—included absenteeism and presenteeism—that is, lost productivity while present at work. Because the greatest number of patients was recruited in France, a societal French costing model based on medication costs, additional physician visit costs, and costs of productivity loss at work was thereafter applied to determine PER and comorbidity-related costs in each treatment group for working patients. All cost figures used were drawn from national official tariff and statistical sources.

TABLE II. Patient demographics

	Placebo (N = 273)	Levocetirizine 5 mg (N = 278)	Total (N = 551)*
Age at randomization, y			
Mean (SD)	30.8 (8.8)	29.8 (8.9)	30.3(8.9)
Median	29.0	28.0	28.2
Minimum-maximum	18.1-70.3	18.0-66.2	18.0-70.3
Duration of PER before randomization, y, mean (SD)	12.8 (8.2)	11.9 (7.8)	12.3 (8.0)
Sex, female	158 (57.9%)	152 (54.7%)	310 (56.3%)
Working status			
Working	196 (72%)	186 (67%)	382 (69%)
Nonworking	77 (28%)	92 (33%)	169 (31%)

*ITT population.

Statistical methods

Patients were recruited in a total of 63 centers, with each center designed to provide 8 to 16 randomized subjects for a total sample size of 500-plus. The primary efficacy analyses were based on the intention to treat (ITT) population by using the analysis of covariance method, with treatment and countries as factors and baseline values as the covariate. Treatment effects were tested on an α level of 5%. No adjustment of the significance level was necessary because a significant result on both primary endpoints was required to have a positive study. RQLQ data were interpreted on the basis of a within-group minimal important difference figure of 0.5.[26] There are various suggestions for between-group minimal important difference figures. In this study, the XPERT board agreed on a 30% difference to placebo as clinically meaningful before unblinding. The sample size of 500 patients allowed the detection of a treatment difference of 1.0 for the T5SS and of 0.36 in the change from baseline for the RQLQ overall score (corresponding to a 40% improvement over placebo, assuming an improvement from baseline for placebo of 0.9) with a 2-sided significance level of 5% and a power of 85%. The bootstrap analysis was used for cost data.[27]

UCB Pharma clinical trials operations monitored the trial and helped in conducting the statistical analyses.

RESULTS

The study randomization started in April 2001 and ended in October 2001. A total of 724 patients were screened at the initial visit, of whom 551 patients were randomized and received I or other study medication. This yielded an ITT population of 551 study subjects, 273 of

TABLE III. T5SS and RQLQ overall score at 4 weeks

Treatment group	N*	Baseline Mean (SD)	After 4 weeks of treatment Adjusted mean (SE)†	Difference vs placebo (95% CI) Adjusted mean	*P* value
RQLQ overall score					
Placebo	252	3.06 (0.94)	−1.01 (0.07)		
Levocetirizine 5 mg	257	3.04 (0.92)	−1.49 (0.07)	0.48 (0.29-0.67)	<.001
T5SS					
Placebo	271	8.90 (2.26)	−2.40 (0.15)		
Levocetirizine 5 mg	276	9.02 (2.28)	−3.54 (0.15)	1.14 (0.75-1.52)	<.001

*Number of ITT patients with nonmissing values at baseline and under treatment.
†Mean change from baseline, adjusted for baseline score and country.

whom were randomized to receive placebo and 278 to receive the study drug. All patients were sensitized to house dust mite and pollen. Further demographic details are shown in Table II.

Overall, 76.4% of patients completed the 6-month study treatment (80.9% levocetirizine and 71.8% placebo, which is commendable considering the size and duration of this allergy trial). Forty-five patients in the placebo group (16.5%) dropped out because of lack of efficacy, compared with 21 (7.6%) in the levocetirizine group ($P = .0007$ for the Wilcoxon test on the time to discontinuation for lack of efficacy). Further explanations included withdrawal of consent for personal reasons (15, 5.5% placebo; 17, 6.1% levocetirizine), adverse events (8, 2.9% placebo; 11, 4.0% levocetirizine) and other justifications (8, 2.9% placebo; 4, 1.4% levocetirizine). One placebo patient was lost to follow-up.

HRQoL

The results for HRQoL as measured by the disease-specific RQLQ overall score at 4 weeks are shown in Table III. There was a larger decrease in RQLQ overall score for levocetirizine compared with placebo (indicating a more important improvement in HRQoL). The adjusted mean reduction for levocetirizine was 1.49 over a period of 4 weeks ($P < .001$), giving an adjusted mean difference versus placebo of 0.48 (95% CI, 0.29-0.67). This difference (47.5% improvement over placebo), which exceeded the predefined minimum clinically meaningful percentage for between-group comparison, is consistent with a significant reduction in symptom severity. In addition, the difference in mean reductions remained statistically significant in favor of levocetirizine for the entire 6 months of the study period, and was also apparent as early as week 1 ($P < .001$). Improvement of the overall score in favor of levocetirizine compared with placebo was confirmed for each RQLQ domain (all *P* values <.001 at 4 weeks; Table IV). The physical and mental component summary scores of the SF-36 followed a similar course, with a larger improvement for levocetirizine group than for placebo at each time point. In the levocetirizine group, mean changes from baseline of the physical and mental summary scores ranged from 3.65 to 5 and from 3.83 to 5.97, respectively, whereas they ranged from 1.61 to 3.37 and from 2.79 to 3.99 in the placebo group. Statistically significant differences were observed between levocetirizine and placebo mean changes after 3 and 4.5 months for the mental component summary score (both *P* values <.01) and after 4 weeks and 3, 4.5, and 6 months for the physical component summary score (all *P* values <.01). Similar to the RQLQ overall score, improvement in the self-perceived health condition appeared linked to symptom relief.

Symptom relief

As with the overall RQLQ score, there was a statistically significant difference in the change from baseline of the mean T5SS over a period of 4 weeks in favor of levocetirizine versus placebo (−3.54 vs −2.40), which equates to an adjusted mean difference of 1.14 ($P < .001$; Fig 1). The difference between the 2 arms of the study was itself larger than the minimum clinically relevant difference versus placebo of 1 that was prespecified by the board of experts. There was a statistically significant difference for the individual symptoms rhinorrhea, sneezing, and nasal and ocular pruritus over a period of 4 weeks of treatment (all *P* values <.001; Fig 1).

Improvements for overall and individual scores were all maintained steady for the entire duration of the 6-month treatment period, and with the exception of nasal congestion, which did not improve significantly before 3 months of treatment, the difference was apparent and statistically significant as early as 1 week after the start of the treatment. Over the period of the first 4 weeks, cromoglycates (both nasal and ocular) were more frequently used in the placebo group (62.6% of the placebo patients vs 49.3% of the levocetirizine patients; $P = .002$). Over the period of the entire 6 months, a trend for more rescue medication use in the placebo group was observed for prednisolone (13.6% vs 10.8%; $P = .362$) and for cromoglycates (75.8% vs 69.4%; $P = .104$).

Pharmacoeconomic assessments

The incidence of all comorbidity events combined over the evaluation period was lower in the levocetirizine group than in the placebo group (54 vs 71 events per 100 patients). The most frequent comorbidities were upper respiratory infections (116 events in the levocetirizine group and 143 events in the placebo group) and asthma (respectively, 20 and 35 events). The absenteeism and

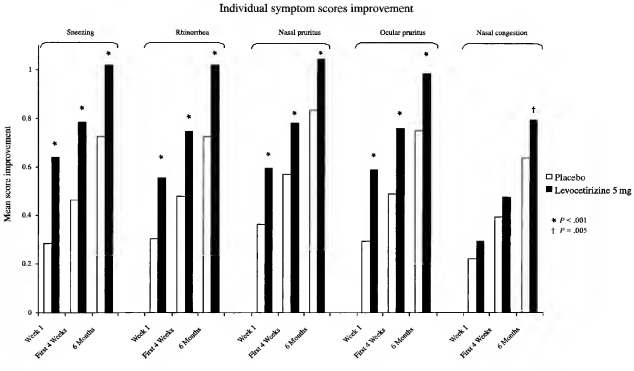

FIG 1. Change in individual symptom scores over a period of 6 months (ITT population).

TABLE IV. Change from baseline of the RQLQ domains at 4 weeks

	Placebo change		Levocetirizine 5 mg change		Difference vs placebo (95% CI)	
Domain	N*	Adjusted mean† (SE)	N*	Adjusted mean† (SE)	Adjusted mean	*P* value
Activities	241	−1.36 (0.10)	248	−2.08 (0.10)	0.73 (0.47-0.99)	<.001
Emotions	252	−0.81 (0.07)	257	−1.16 (0.07)	0.35 (0.17-0.54)	<.001
Eye symptoms	252	−0.91 (0.09)	257	−1.40 (0.09)	0.48 (0.26-0.70)	<.001
Non–hay fever symptoms	252	−0.83 (0.08)	257	−1.21 (0.08)	0.38 (0.18-0.57)	<.001
Nasal symptoms	252	−1.10 (0.09)	257	−1.64 (0.09)	0.54 (0.31-0.77)	<.001
Practical problems	252	−1.50 (0.10)	257	−2.06 (0.10)	0.56 (0.30-0.82)	<.001
Sleep	252	−0.86 (0.09)	257	−1.35 (0.09)	0.50 (0.27-0.73)	<.001

*Number of ITT patients with nonmissing values at baseline and under treatment.
†Mean change from baseline, adjusted for baseline score and country.

presenteeism, expressed in days per month per patient, were lower in the levocetirizine group (0.18 vs 0.45 days in absenteeism and 0.70 vs 1.1 days in presenteeism). No hospitalization was reported.

After applying a French societal costing model to levocetirizine and placebo group outcomes, the combined direct cost (including levocetirizine costs) and indirect cost categories for PER and comorbidity were 160.27€ per working patient per month for the placebo group and 33% lower for the levocetirizine group at 108.18€ per working patient per month ($P = .008$). Table V shows detailed costs by treatment group.

Adverse events

Levocetirizine appeared to be safe and well tolerated, particularly considering the length of the treatment. In the placebo group, 193 (70.7%) patients, compared with 192 (69.1%) in the levocetirizine group reported at least 1 adverse event at some point during the 6-month study. The most common adverse events were headache (23.2% placebo vs 24.5% levocetirizine), pharyngitis (20.5% and 19.8%, respectively), influenza-like symptoms (13.9% vs 14.0%), fatigue (7.0% vs 8.6%), somnolence (1.8% vs 6.8%), and gastroenteritis (5.1% vs 2.9%).

DISCUSSION

Following the recent ARIA initiative, this study attempts to provide a benchmark for future rhinitis trials, both in terms of definition of allergic rhinitis, its size (over 550 patients), its comprehensive study design (validated HRQoL and health status measures, symptom scores, electronic diary capture), and its exceptional duration (26-week treatment phase). Under the formerly used rhinitis

TABLE V. Mean direct and indirect costs per month per working patient

	Placebo mean € (95% CI) (N = 196)	Levocetirizine 5 mg mean € (95% CI)(N = 186)	Difference vs placebo	*P* value
Direct costs				
Total direct medical costs for PER	5.32€ (4.43, 6.42)	16.81€ (15.94, 18.13)	11.50€ (10.06, 13.03)	<.001
Total direct medical costs for comorbidities	2.72€ (1.82, 4.20)	1.77€ (1.14, 3.04)	−0.96€ (−2.60, 0.40)	.18
Indirect costs				
Absenteeism	45.70€ (32.02, 75.00)	18.57€ (13.75, 26.00)	−27.14€ (−55.78, −12.10)	<.001
Presenteeism	106.54€ (86.97, 132.86)	71.04€ (56.16, 92.43)	−35.50€ (−65.21, −7.01)	.02
Total costs	160.27€ (129.93, 204.54)	108.18€ (91.55, 131.78)	−52.09€ (−98.18, −13.26)	.01

classification system, *seasonal* rhinitis studies typically lasted 2 weeks and *perennial* rhinitis trials normally 4 weeks. Because it was large and lasted 6 months, the XPERT study clearly offers more meaningful and inherently more credible insights into the management of PER and its frequently debilitating symptoms. The concept of minimal persistent inflammation implies that although patients with persistent allergic rhinitis have varying allergen exposure throughout the year, even during periods when they might be symptom-free, these patients can still have inflammation in the nose.[28] For such patients, long-term therapy might be desirable if it successfully improves symptoms that significantly degrade their perceived HRQoL and their productivity in society, as investigated in this study. The advantages of a long-term and continuous therapy with antihistamines have been formerly demonstrated in children, in whom a 6-month treatment was able to reduce both rhinitis and comorbid diseases.[29]

As far as levocetirizine itself is concerned, it appears to be effective over extended periods, and most of the benefits are maintained for as long as therapy is continued. Furthermore, statistically significant relief was available within a week for almost all of the cardinal symptoms. Even nasal congestion—in which reversal of established mucosal inflammation is required and traditional antihistamines are acknowledged to be less effective—was eventually brought under control. It is not clear why this particular aspect of relief took about 3 months to develop, but it may be a result of a longer-term anti-inflammatory action of levocetirizine. In terms of adverse events, for the most part, levocetirizine appeared to give rise to a number and type of events similar to placebo with the exception of a higher, though still low, incidence of somnolence. At first sight, many adverse events in both arms seemed to occur in greater absolute percentages of patients than might be anticipated. However, most of this excess can be explained by the exceptionally long duration of the study, with the probability of having an adverse event obviously higher in a 6-month study compared with a study of 2 to 4 weeks.

Further analyses revealed that the relative duration of sedating events (adverse events reported as being "fatigue," "asthenia," or "somnolence") in the ITT population was similar in the 2 groups (3.26 days per 100 days of treatment in the placebo group vs 3.72 days per 100 days of treatment in the levocetirizine group). The mean duration of sedating events per subject was longer in the placebo group (42.26 days per 100 days of treatment) than in the levocetirizine group (25.31 days per 100 days of treatment).

Health-related quality of life was not altered by the somnolence rate observed in the levocetirizine group, as indicated by the larger improvement reported in this group at all time points for the RQLQ overall score. More specifically, the RQLQ domain including items such as fatigue or tiredness (ie, the nonhayfever symptoms domain) also showed a larger improvement in the levocetirizine group than in the placebo group.

This study seems to support the correctness of the ARIA classification and validates the concept of persistent disease in a distinct and numerically large subset of rhinitis patients, who have symptoms sufficiently to impair their quality of life both in season and out of season. In such patients, effective long-term treatment results in an equally persistent improvement in quality of life and health status as measured by 2 reliable instruments, 1 specifically tailored to measure the effect of allergic rhinitis (RQLQ) and 1 generic and allowing comparison with other diseases (SF-36). Thus, the symptom scores tie in with the HRQoL results, insofar as placebo patients continued to have heavier symptoms and to report poorer HRQoL compared with patients receiving levocetirizine, with the benefits of active therapy maintained for as long as the treatment was given.

Effective long-term treatment with levocetirizine also appears to deliver an overall reduced disease burden in terms of overall costs (direct and indirect costs) for PER itself and associated comorbidities. Because most patients in this study were recruited in France, a specific societal French costing model was used to estimate direct medical costs (drug costs, intervention costs) and indirect costs (work productivity losses) by using official drug/physician pricing and average earnings statistics. Therefore, although the specific cost savings determined may vary between countries, as may the figure of an overall 33% reduction in disease costs with active treatment, it seems likely that effective therapy of PER will produce monetary benefits for the society. As expected from the HRQoL results, the levocetirizine group scored more favorably in

pharmacoeconomic parameters, translating the improved well-being into practical socioeconomic benefits.

Levocetirizine appears to be a rapidly and sustainably effective antihistamine for the treatment of PER and provides statistically significant and clinically meaningful improvements of symptom scores, overall HRQoL, and pharmacoeconomic criteria, which are some of the key criteria for the successful treatment of a chronic disease.

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